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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,706	02/26/2002	Poul Baad Rasmussen	0228us410	7876

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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 01/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,706	RASMUSSEN ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *88,89,92,94-99 and 109-117* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *88,89,92,94-99 and 109-117* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to the amendment and remarks filed on 10/4/2005. Claims 100-108 have been withdrawn. Claims 90, 91 and 93 have been cancelled. Claims 88-89 and 92 have been amended. New claims 109-117 have been added. Claims 88-89, 92, 94-99 and 109-117 are pending and the subject of this action.

2.The Examiner had previously discussed (12/20/2005) the possibility of allowing the pending claims with the Applicants representative, an interview summary is enclosed.

3. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

4. The rejection of claims 88-89, 92, 94-99 and 109-117 (newly added), under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter is maintained. Applicants' arguments have been fully considered but not found to be persuasive because it is not clear what is the correlation between the variants (up to 15 amino acid changes in SEQ ID NO: 2) and the interferon-β activities (antiviral, antiproliferative or immunomodulatory). It is not clear if the variants will posses all or some of the activities of the wild type protein. Claims 89, 92, 94-99 and 109-117 are rejected insofar as dependent on rejected claim 88.

5. The rejection of claims 88-89, 92, 94-99 and 109-117 (newly added) under 35 USC 112, 1st paragraph, as containing subject matter that was not clearly described in the specification is maintained for reasons set forth in the pages 3-5 of the Office Action

dated 4/5/2005. Applicants' arguments have been fully considered but are not found to be persuasive because it is not clear if the Applicants were in possession of interferon-β variants that have no more than 15 amino acid changes and contain interferon-β activity. The Examiner takes no position with Applicants discussion on the relevant case law on pages 9-10 the response.

Applicants argue that (1) each of the claims specifies an IFN-β polypeptide variant exhibiting IFN-β activity. (2) The specification clearly defines such activity and describes methods for determining whether an IFN-β polypeptide variant exhibits IFN-β activity. In addition, Applicants assert that examples 5 and 6 demonstrate IFN-β activity. The specification, discloses the antiviral activity of the K19R+K45R+K123R variant (see example, 13). These are not found to be persuasive because what specific IFN-β activity such as antiviral, antiproliferative or immunomodulatory is conferred by the various variants is not disclosed.

Contrary to Applicants' assertions (pages 12-13, of the response filed 10/4/05), while the specification discloses variant IFN-β with two N-glycosylation sites, it does not disclose IFN-β activity that is specific. In addition, it does not certainly disclose variants with up to 15 amino acid changes (including the two glycosylation sites) with any of the specific activities recited above. Specifically, there is no correlation between the variants and the IFN-β activities. MPEP2163 [R-2] states that "The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its

function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence". In the instant invention, Applicants have described potential amino acid changes with no correlation to IFN-β activities. Therefore, the rejection of record is maintained. Claims 89, 92, 94-99 and 109-117 are rejected insofar as dependent on rejected claim 88.

6. The rejection of claims 88-89, 92, 94-99 and 109-117 (newly added) under 35 USC 112, 1st paragraph, while being enabling for an interferon-β variant with substitutions at K19R+K45R+K123R of the wild type protein which has antiviral activity (see page 107 of the specification), the disclosure does not reasonably provide enablement for all variants interferon-β contemplated is maintained for reasons set forth in the Office Action dated 4/5/2005 pages 4-8.

Applicants assert that the amended claim 88 and the dependent claims are enabled because, claim 88 specifies an IFN-β polypeptide variant exhibiting IFN-β activity which comprises a variant sequence which differs from the wild-type human IFN-β sequence SEQ ID NO: 2 in no more than 15 amino residues (see top of page 16, specification). Although, the Applicants assert that the specification provides detailed guidance with respect to variants and the specific activities associated with variant (up to 15 amino acid changes), there is no guidance in the specification correlating activity (antiviral or antiproliferative or immunomodulatory). Although, Applicants have provided

several examples in the specification of generating variants, there is no correlation of IFN-β activity provided. For example, it is not clear how multiple amino acid changes (15/166 or 10%) within the polypeptide will affect the activities of the protein. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. As discussed in the Office Action dated 4/5/2005, although the specification outlines art-recognized procedures for producing and screening for active variants, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Thus, in the absence of guidance in the specification to the correlation of IFN-β activities to specific mutations, and the breadth of possible changes, nor would it be predictable to the artisan how to make a functional IFN-β variant especially in light of a specific IFN-β activity recited in the claims, it would require undue experimentation of one skilled in the art. Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Thus, the pending rejections are maintained. Claims 89, 92, 94-99 and 109-117 are rejected insofar as dependent on rejected claim 88.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7a.Claims 88, 89, 92, 94-99 and 109 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 10, 17, 18,19 and 22-24 of U.S. Patent No. 6, 531, 122 in view of Apweiler et al. (1999).

The instant invention is drawn to IFN-β variants (no more than 15 amino acid changes in SEQ ID NO: 2) with at least one introduced N-glycosylation.

Pedersen et al. (U.S. Patent No. 6, 531, 122) disclose IFN-β variants exhibiting IFN-β activity, comprising a variant sequence, which differs from the wild type human IFN-β sequence SEQ ID NO: 2 in no more than 15 amino acid residues. However, the claims do not specifically recite N-glycosylation at sites Q49N+Q51T/S and F111N+R113T/S.

Apweiler et al. (1999) disclose the N-glycosylation consensus sequence NXS/T (where X can be any amino acid but proline) required for N-glycosylation of protein. Therefore, it would have been *prima facie* obvious at the time of the invention to

generate N-glycosylated IFN-β because Apweiler et al. reference identifies the consensus sequence required for N-glycosylation. One of ordinary skill in the art would have been motivated to generate N-glycosylated because of the stability of the protein. Therefore, the instant invention are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 10, 17, 18,19 and 22-24 of U.S. Patent No. 6, 531, 122 in view of Apweiler et al. (1999).

8. No claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSS 1/06

ROBERT S. LANDSMAN, PH.D
PRIMARY EXAMINER